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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,327	05/15/2002	Jay M Meythaler	UAB-15102/22	3596

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EXAMINER	
WILLIAMS, LEONARD M	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
11/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/049,327	MEYTHALER ET AL.	
	Examiner	Art Unit	
	Leonard M. Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,29,34-36 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 7, 29, 34-36 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Response to Amendment/Argument

Applicant's amendment received 07/11/2007 amending claims 1, 7, 29, 34, 36 and 40; and canceling claims 4-6, 30-33, 37-39, 41 and 42 has been entered. Claims 1, 7, 29, 34-36 and 40 are currently pending.

Applicant's arguments with respect to claims 1, 7, 29, 34-36 and 40 have been considered but are moot in view of the new rejections necessitated by applicant's amendments.

The applicant's amendment of claims 1, 7, 29, 34, 36 and 40 remove reference to a non-steroidal, anti-inflammatory salicylate drug (NSAID) and to specifically include choline magnesium trisalicylate and administration intrathecally by intrathecal catheter into the claims. These limitations have been addressed in the previous office action as written. As such the rejections of the previous office action have been modified to address the claim amendments (cancelled claims). The modified rejections are detailed below.

The examiner respectfully notes that choline magnesium trisalicylate is considered a non-steroidal, anti-inflammatory salicylate drug (NSAID).

The applicant's have asserted on page 6 of the remarks that at best the teaching of Myseros et al. provides a "motivation to try" and thus is an insufficient basis to maintain an obviousness-type rejection. The examiner respectfully disagrees. As set

forth in then rejection Myseros et al. teach the use of glutamate antagonist in a fluid percussion model of traumatic brain impact. The glutamate antagonist resulted in a dose-dependent improvement in both mortality and memory and motor tasks. Thus there is no "motivation to try" there is clear and objective evidence in an accepted animal model of traumatic brain trauma that administration of glutamate antagonists results in a dose-dependent improvement of symptoms. There is no conjecture about whether the compounds would be active or could be active, only an animal model demonstrating such activity.

The applicants have amended the claims to include a method for treating a subject having inflammation associated with neurotrauma. The applicant's have previously asserted that the prior art references teach away from the treatment of neurotrauma via administration of non-steroidal anti-inflammatory analgesics (NSAIDs) in a subject having inflammation associated therewith. The examiner respectfully disagrees. The examiner respectfully points out that Grilli et al. teaches, on page 3, that the hypothesis that inflammatory processes contribute to the pathology of neurodegenerative diseases...is supported by clinical and epidemiological studies. Thus Grilli et al. clearly implicates inflammation as an aspect in the treatment of neurodegenerative diseases with NSAIDs. The examiner respectfully points out that even if the prior art did teach treatment of neurotrauma, with no association with inflammation, via administration of a non-steroidal anti-inflammatory analgesic (NSAID); the NSAIDs still possess anti-inflammatory properties inherently and thus would still treat any inflammation associated with the neurotrauma as claimed.

"Products of identical chemical composition can not have mutually exclusive properties. "A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

For the reasons detailed above and for reasons of record the rejections of the prior office action are modified to reflect the applicant's amendments to the claims. No new art has been used. No claims are allowed. This action is made **final**.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 7, 29, 34-36 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grilli et al. (WO 98/20864), in view of Bakhshi et al. (*Journal of Neuro-Oncology*, 26, 133-9), in view of Myseros et al. (The rationale for glutamate antagonists in the treatment of traumatic brain injury, Ann NY Acad Sci, 1995, 765:262-271) and further in view of McGeer et al. (USPN 5192753).

Grilli et al. teaches the treatment of Alzheimer's disease through the use of NSAIDs (Abstract). Sodium salicylate and salicylamide are specifically taught as NSAIDs useful in the invention disclosed therein (p 3). Neuronal damages (i.e.

neurotrauma or neuronal injury) related to Alzheimer's disease are specifically taught as treatable by the NSAIDs disclosed therein (p 6). Generally, cranial and spinal traumas are also taught to be treatable by the methods disclosed (p 6). Grilli et al. teach, on page 5, that non-steroidal anti-inflammatory drugs can be used in the prevention and/or treatment of glutamate receptor-mediated neuronal damages, independently of any anti-inflammatory properties. Further the NSAIDs show a protective activity against glutamate-induced neurotoxicity. Grilli et al. lacks a specific teaching of the claimed NSAID-choline magnesium trisalicylate, the mode of administration and a specific teaching of the treatment of neurotrauma associated with traumatic brain injury (i.e., traumatic brain trauma and diffuse axonal injury associated with such).

Bakhshi et al. teaches the administration of CNS drugs via intrathecal catheter. Such administration is taught to alleviate adverse systemic effects, peripheral metabolism of centrally acting drugs, inadequate blood-brain barrier penetration, etc. See page 133. Administration of drugs effective for treating Alzheimer's disease is specifically taught as useful in this manner. See page 137.

Myseros et al. teach, on page 262, that excitotoxic damage to neurons and glia may develop as a consequence of excessive release of excitatory amino acids after primary impact injury, ischemic events, and hematoma. Further it appears that glutamate antagonists have potent neuroprotective effects for head-injured patients. On page 263, Myseros et al. teach that diffuse axonal injury is a process that does not occur instantaneously after a traumatic brain event, but rather that after impact an immediate and massive release of neurotransmitters (including glutamate) is noted and

structural axonal disruption occurs later. Myseros et al. teach, on page 264, that the structural axonal lesions seen after sheer injury may not be caused by a mechanical process, but by a failure of ionic homeostasis mediated via the glutamate channel. Further, on page 265, Myseros et al. teach that treatment of rats with a glutamate antagonist in the fluid percussion model (an animal model for traumatic brain impact and associated diffuse axonal injury) results in a dose-dependent improvement in both mortality and memory and motor tasks.

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer the composition of Grilli et al. for the treatment of Alzheimer's disease (and any neuronal damage associated therewith) and neurotrauma (specifically traumatic brain injury and associated diffuse axonal injury) because (1) Grilli et al. teaches the administration of the composition for said treatment generally (and that said compounds can be used in the prevention and/or treatment of glutamate receptor-mediated neuronal damages); (2) Bakhshi et al. teaches the administration of drugs to the CNS for the treatment of Alzheimer's Disease via intrathecal catheter and (3) Myseros et al. teach that prevention and/or treatment of glutamate neurotoxicity (specifically by glutamate antagonists) results in improvement in both mortality and morbidity of patients. One would have been motivated to administer the composition of Grilli et al. by intraventricular or intrathecal injection, facilitated by catheter, because of an expectation of success in treating neuronal damage associated with Alzheimer's, as taught by Grilli et al. and in treating neurotrauma as taught by Myseros et al.; an expectation of success in alleviating adverse systemic effects associated with the

administration of the drug, ensure adequate blood-brain barrier penetration, etc., as taught by Bakhshi et al.

McGeer et al. teaches arylcarboxylic acids such as salicylic acid, acetylsalicylic acid, choline magnesium trisalicylate, salicylate, etc. as equivalent NSAIDs useful for the treatment of Alzheimer's disease (col. 1, lines 36-65).

It would have been obvious to one of ordinary skill in the art to utilize the specific NSAID choline magnesium trisalicylate in a method of Grilli et al. and Bakhshi et al. because (1) Grilli et al. teaches the use of derivatives of acetylsalicylic acid as NSAIDs useful for the treatment of neuronal damage associated with Alzheimer's disease; (2) Grilli et al. teaches that salicylates and pharmaceutical acceptable salts thereof are useful as NSAIDs in the treatment of neuronal damage associated with Alzheimer's disease; and (3) McGeer et al. teaches that choline magnesium trisalicylate is a salicylate suitable for the treatment of Alzheimer's disease. One would have been motivated to utilize the specific salicylate choline magnesium trisalicylate because of the expectation of success in treating neuronal damage associated with Alzheimer's disease by administering a derivative of acetylsalicylic acid to a patient in need thereof, as taught by Grilli et al. and due to McGeer et al's. demonstration of the equivalence of choline magnesium trisalicylate, acetylsalicylic acid and salicylic acid.

It is noted that the recitation of the limitation of "non-inhibitory of platelets" is a recitation of a limitation as to the property of the drug. It is also noted that the recitation provides no information as to how it would limit the structure of the claimed NSAIDs. Accordingly, since Examiner has shown that it is known to administer the same

compositions as instantly claimed, the compositions would obviously be non-inhibitory of platelets. A compound and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M. Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LMW